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ASIA EDITION

Singapore's Duke-NUS research unlocks precision therapy for drug-resistant leukaemia

07 November 2024 | News

The findings could have a profound impact on precision oncology treatments administered by triggering the BIM protein kill tumour cells

Scientists from Singapore's Duke-NUS Medical School and their collaborators have identified an inherited genetic variation prevalent among East Asians that contributes to drug resistance, driving the aggressive growth of cancer cells in patients with chronic myeloid leukaemia.

Team’s pioneering approach involves inhibiting the action of a protein called MCL-1, with laboratory studies showing promising results in effectively killing cancer cells resistant to conventional treatments. These findings, demonstrate the importance of genetic profiling to develop precise and more effective treatments for patients with cancer.

One sixth of human cancers harbour genetic variations but few studies have established how that affects treatment outcomes. The team sought to answer this question by honing in on an inherited genetic variation that affects patients with leukaemia.

The Duke-NUS scientists, in collaboration with their partners, including Singapore General Hospital and The Jackson Laboratory, developed the first pre-clinical model with a common genetic variation among the population of the East Asian region, which includes Chinese, Japanese and Korean people. About 12 to 15 per cent of people from this region carry an inherited genetic variation in a protein called BCL-2 interacting death mediator (BIM), which is crucial for regulating cell death to eliminate damaged or unwanted cells. Many cancer treatments trigger this process to destroy tumour cells.

Discoveris with a pre-clinical model, showing that the variation results in the production of alternative versions of the BIM protein, which, in turn, helps cancer cells evade cell death. Consequently, the tumour cells survive longer and are able to multiply more aggressively, contributing to disease progression.

Duke-NUS Associate Professor Charles Chuah, a Senior Consultant at the Department of Haematology, Singapore General Hospital and National Cancer Centre Singapore, collaborated on the study said, "Given the prevalence of the BIM variation in

the East Asian population, it is crucial to understand its impact on cancer treatment. Our findings suggest that genetic testing for this variant at diagnosis can improve outcomes by identifying patients who may benefit from more aggressive treatments."